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UNITED STATES GOVERNMENT

Memorandum

TO : Petitions Control Branch

DATE: February 24, 1966

FROM : Dr. G. E. Whitmore G. E. W.
Division of Toxicological Evaluation
Petitions Review Branch

SUBJECT: Pyrethrins, Piperonyl Butoxide, MGK 264 (N-octylbicycloheptane dicarboximide)

FOOD ADDITIVE PETITION NO. 6H1946

McLaughlin-Gormley-King Co.
Minneapolis, Minn. 55414
(AF 8-176)

MGK rat reproduction study:

By Industrial Biological
Laboratories, Inc.

Twenty (20) female and ten (10) male weanling Sherman-Wistar strain rats in each group exposed to 0.0%, 0.0035%, 0.035%, and 0.35% diets of MGK. Breeding began at the age of 100 days. The first litters were raised to weaning-20 female and 10 male randomly selected for parents of the 2nd generation. This breeding scheme was similarly used to produce the 3rd generation. Two (2) weanlings each of the 3rd generation second litters, control and 0.35% diet groups*, were necropsied and histopathological examination made of the brain, lung, heart, spleen, bone marrow, stomach, small intestine, large intestine, pancreas, liver, kidney, gonads, skin, and bone. Compound related changes were absent in the examined tissues.

Growth and food consumption of parents in each generation was uninfluenced by compound ingestion. Differences found at specific times in particular groups were not significant when related to the total data.

Gross external examination of all weanlings disclosed no birth defects. Two (2) weanlings from each litter were autopsied for evidence of compound produced related effects. None were found.

BREEDING HISTORY

% Diet	Litter	No. Female in Group			No. Litters Born		
		P1	P2	P3	P1	P2	P3
0.0	1	17	20	18	17	20	18
	2	17	20	18	14	14	12
0.0035	1	17	20	20	17	19	19
	2	17	20	20	11	6	17
0.035	1	19	20	20	18	17	20
	2	19	20	20	12	11	16
0.35	1	18	19	19	15	19	19
	2	18	19	19	7	12	17

*One of each sex from each litter except, 2 males from 0.35% rat #15, one female from 0.35% rat #16, one female from 0.35% rat #17, and one male from 0.35% rat #18.

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SURVIVAL RECORDS - Average Litter size

% Diet	Litter	Alive at birth			Alive at 4 days			Alive at weaning		
		P1	P2	P3	P1	P2	P3	P1	P2	P3
0.0	1	9.2	10.3	10.2	9.3	9.8	10.2	8.8	9.1	10.2
	2	10.2	10.9	11.7	10.1	10.5	11.5	10.0	9.1	11.3
0.0035	1	9.9	10.0	11.1	9.9	10.0	10.9	9.6	8.0	10.4
	2	11.5	11.1	11.3	11.3	10.8	10.9	10.5	9.0	10.8
0.035	1	10.2	8.6	10.3	10.1	8.5	9.7	10.0	8.3	9.7
	2	10.7	10.1	10.6	10.6	9.5	9.8	10.3	8.4	9.3
0.35	1	10.5	7.9	10.3	9.4	7.8	10.1	9.3	7.1	10.1
	2	11.5	10.7	10.6	11.5	10.6	10.3	11.0	9.5	10.3

WEIGHT RECORDS (grams) Average per Litter

% Diet	Litter	Litter weight 24 hours			Litter weight at 4 days			Litter wei weaning		
		P1	P2	P3	P1	P2	P3	P1	P2	P3
0.0	1	72	75	73	105	105	112	415	389	46
	2	70	79	80	112	118	114	436	421	49
0.0035	1	79	67	79	111	108	117	469	337	46
	2	84	75	80	123	115	113	466	424	491
0.035	1	78	63	78	113	93	108	424	353	456
	2	77	67	72	115	101	93	415	380	413
0.35	1	81	57	79	100	78	110	360	309	413
	2	84	74	78	123	107	114	430	400	457

I N D I C E S

% Diet	Litter	P1 Viability	P1 Lactation	*Growth Ratio
0.0	1	90	99	3.67
	2	99	96	3.53
0.0035	1	99	99	3.79
	2	99	97	3.65
0.035	1	99	98	4.19
	2	98	93	3.81
0.35	1	99	95	4.08
	2	100	98	3.97
		P2		
0.0	1	95	85	3.61
	2	99	89	3.64
0.0035	1	98	89	3.83
	2	89	90	3.82
0.035	1	100	80	3.04
	2	98	90	3.88
0.35	1	92	94	3.78
	2	98	84	3.54
		P3		
0.0	1	99	99	3.85
	2	98	100	4.12
0.0035	1	89	100	4.20
	2	93	95	4.49
0.035	1	99	96	4.04
	2	96	99	4.41
0.35	1	100	100	4.18
	2	98	98	4.33

*Growth ratio - Ratio of average litter weaning weights to average litter weights at 4 days.

The above summary tables of the reproduction performance for 3 generations of rats on 0.0%, 0.0035%, 0.035%, and 0.35% diets of MGK 264 are lacking in evidence of compound related effects. A 'no effect' diet level of 0.35% (3500 ppm) has been demonstrated in this rat reproduction study.

The two year 300 ppm no effect swine feeding study (July 15, 1965), the two year 1000 ppm no effect rat feeding study (Jan. 18, 1965 memo), and this 3500 ppm no effect rat reproduction study, demonstrating the non toxicity of MGK 264 at the fed levels, allows a decision that granting a 10 ppm residue tolerance of MGK 264 when used with pyrethrin and piperonyl butoxide as requested by this petition, would be non-hazardous.

FAP #227, 404

INIT: HBlumenthal 2/28/66

cc: TE
FSA (Pesticides Br)
FAP No. 6H1946

GEWhitmore:smr 2-24-66

OPP 3/4/66